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Role of fruit and vegetables in sustaining healthy cognitive function: evidence and issues

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Modifiable lifestyle factors, such as improved nutrition, are crucial in maintaining cognitive health in older age. Fruit and vegetables represent healthy and sustainable sources of nutrients with the potential to prevent age-related cognitive decline. The aim of this review is to synthesise the available evidence, from epidemiological and randomised controlled trials (RCT), regarding the role of fruit and vegetables in sustaining healthy cognitive function. Epidemiological studies of combined fruit and vegetable intake suggest that increased consumption may sustain cognition in later life. The evidence appears to be stronger for an association between vegetables and cognition, particularly for green leafy and cruciferous vegetables. Specific benefits shown for berries, citrus fruits, avocado and nuts suggest fruit is worthy of further investigation in relation to cognition. Data from RCT indicate benefits to differing aspects of cognition following citrus and berry fruits, cocoa and peanuts, but the data are limited and there are a lack of studies exploring effects of vegetables. There is growing evidence for an association between fruit and vegetable intake and cognitive function, but this is not always consistent and the data from RCT are limited. Issues in previous research are highlighted, such as strict exclusion criteria, absence of baseline nutritional status data and lack of consideration of individual differences, which may explain the weaker findings from RCT. Inclusion of those most at risk for cognitive decline is recommended in future nutrition and cognition research.

Fruit and vegetables: Diet: Cognitive decline: Ageing

The world's population is ageing. By 2030, one in six people will be aged 60 years or over[1]. However, average health span is not increasing at the same rate as lifespan, as indicated by the increasing prevalence of non-communicable diseases such as CVD and diabetes. Of relevance to this review, dementia has recently emerged as the leading cause of death in the UK. In 2019, one in every fourteen of the UK population aged 65 years and over were diagnosed with dementia[2], and globally this condition affects more than twice as many women as men[3]. Despite the high prevalence and significant impact of dementia, such as Alzheimer's disease, there are currently no effective pharmaceutical treatments to slow down or reverse disease progression. It is, therefore, imperative that we develop ways to prevent, or at least delay, dementia and maintain cognitive health into older age.

Nutrition represents a crucial modifiable lifestyle factor in the quest to sustain health, including healthy cognitive

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Abbreviation: RCT, randomised controlled trial.
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function. The importance of nutrition is evident from the inverse relationships between non-communicable diseases and adherence to healthy dietary patterns such as the Mediterranean diet, dietary approaches to stop hypertension diet, the Mediterranean-dietary approaches to stop hypertension intervention for neurodegenerative delay, the Nordic diet and the traditional Asian diet[4]. In fact, dietary risks were observed to be the leading cause of disease burden in the United States between 1990 and 2010[5], with a low intake of fruit, vegetables and nuts listed in the top five leading dietary risk factors for death and disability-adjusted life years globally[6]. CVD was cited as the leading cause of diet-related death and disability-adjusted life years, highlighting the importance of dietary factors to cardiovascular health. Cardiovascular risk factors are also linked to cognition. For instance, high cholesterol at midlife is associated with an increased risk of vascular dementia[7], as well as accelerated cognitive decline, including a specific association for LDL-cholesterol[8]. Hypertension has been linked to dementia[9], including Alzheimer's disease[10], as well as steeper cognitive decline[11] and poor cognitive function[12]. There is also evidence for race[11] and sex differences[13] in these relationships. Prior to hypertension, arterial stiffness is associated with worse cognitive outcomes in older adults, and in midlife[14]. Low-cardiac output, which data from the Framingham Heart Study Offspring Cohort indicate one-third of the general adult population meets clinical criteria for[15], is associated with worse cognitive performance[16]. This is potentially mediated by the corresponding cerebral blood flow reductions observed in cardiac dysfunction, which can lead to synaptic dysfunction[17] and blood–brain barrier permeability[18]. Increased risk of dementia[19] and accelerated cognitive decline[20] are also observed in type-2 diabetes, which may be due to increased blood–brain barrier permeability[21]. Blood–brain barrier disruption has been linked to inflammation[22,23], which can increase the risk of atherosclerosis and insulin resistance[24]. Potential mechanisms of increased inflammation in older age and in chronic conditions include changes to gut microbiota and gut permeability[25], which are also linked to brain function[26] and to mental health conditions including depression[27]. The risk factors outlined all have the potential to be impacted by diet and could therefore represent mechanisms for dietary effects on cognition. Obesity is also associated with a pro-inflammatory state[25], highlighting the role of diet, which is supported by studies showing beneficial effects of anti-inflammatory diets[28,29].

In meta-analyses, adherence to the Mediterranean diet was associated with better global cognition both cross-sectionally and longitudinally[30], whilst intervention with a Mediterranean diet was shown to improve cognition when compared to a low-fat control diet[31]. One aspect that is common across healthy diet patterns such as the Mediterranean, dietary approaches to stop hypertension and Mediterranean-dietary approaches to stop hypertension intervention for neurodegenerative delay diets, is the recommendation to increase intake of fruit and vegetables. The EAT-Lancet commission report[32], which highlights food as the greatest prospect to optimise health and environmental sustainability, also recommends increased fruit and vegetable intake to improve human and planetary health. A recent review of the EAT-Lancet reference diet and cognition across the life course concluded that the current evidence base is weak, but high fruit and vegetable intake seems to benefit cognition, particularly in older adults[33].

The aim of this review was to synthesise the evidence for fruit and vegetable intake to sustain cognition in cognitively healthy older adults, and to highlight challenges in this field of research. One issue that is immediately apparent is the use of dementia screening tools, such as the mini-mental state examination, to assess cognition in cognitively healthy older adults. Due to the lack of sensitivity of these screening tools, this review will focus on studies that include measures of cognitive function. One of the most studied aspects of age-related cognitive decline is episodic memory, which reflects the ability to store and subsequently retrieve, and to recognise, previously presented verbal, visual or spatial information. Another aspect of cognition that deteriorates with age is executive function. This involves complex or higher order thinking such as planning, problem solving and reasoning, and is underpinned by working memory as well as information processing. Sustained and selective attention are also important cognitive domains, which respectively reflect the ability to maintain attention on a stimulus or a task for a long period, and the ability to respond to relevant stimuli (targets) whilst ignoring irrelevant stimuli (distractors). One of the difficulties here is that cognitive tasks are often mixed, so there is overlap in terms of the domains involved. For example, the Stroop task involves aspects of executive function whilst also assessing selective attention. (See Table 1 for summary and evaluation of key cognitive domains.)

In the following sections, data on the relationship between fruit and vegetable intake and cognitive performance are reviewed, followed by a review of randomised controlled trials (RCT) exploring the impact of daily fruit and vegetable intake on cognitive function in healthy older adults.

Epidemiological evidence

Epidemiological studies in this area that have focused on fruit and vegetables as a combined category have shown some positive findings. In the Whitehall II study, consuming <2 portions of fruit and vegetables daily was associated with an increased risk of poor executive function and, to a lesser extent, poorer episodic memory[34]. This association was apparent for fruit and vegetable intake at midlife but was strongest when measured cross-sectionally at 15-year follow-up. The supplementation with antioxidant vitamins and minerals 2 study also showed that higher fruit and vegetable intake was associated with better verbal memory at 13-year follow-up, with specific effects for fruit and for vitamin C-rich fruit and vegetables[35]. However, in this study the association with executive functioning was negative. One possible explanation for the discrepancy in findings relating

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Table 1. Summary and evaluation of key cognitive domains

Cognitive domain	Task requirements	Task examples	Evaluation
Episodic memory	Ability to store and subsequently retrieve, and to recognise, previously presented verbal, visual or spatial information	Immediate and delayed word recall, word recognition, paired associates learning test, letter memory, verbal memory tasks, object recognition, Corsi blocks task	Overlap in domains measured via tasks, scores on different tasks often do not correlate despite measuring the same domain
Executive functions	Complex or higher order thinking such as planning, problem solving and reasoning	Task-switching test, trail-making test, Stroop task	Overlap in domains measured via tasks, studies often do not measure all sub-domains of executive function as this is not done in one task, tasks are very susceptible to age, education and socioeconomic status
Working memory	Retaining information temporarily to use for more complex cognitive functions	Numeric working memory task, digit span, spatial working memory task, Corsi blocks, serial subtractions, Sternberg memory scanning, trail-making test	
Information processing	Decoding incoming information and formulating a response	Rapid visual processing task, Stroop task, letter digit substitution test	
Sustained attention	Direct and focus cognitive activity on specific stimuli	Attention network task, rapid visual processing task, sustained attention task	Overlap in domains measured via tasks, only small to moderate correlations found between psychological measures of sustained attention and behavioural ratings
Selective attention	Select and focus on a particular stimulus for further processing whilst simultaneously suppressing irrelevant information	Stroop task, modified attention network task, selective reminding test	Overlap in domains measured via tasks, some tasks have low construct validity and external validity

to executive function is the classification of verbal fluency as memory tasks in the supplementation with antioxidant vitamins and minerals 2 study[35], whereas this was categorised as executive function in the Whitehall II study[36]. It is also important to note that in both studies no measure of cognition was taken at baseline, so assessment of cognitive decline was not possible. Support for a relationship between fruit and vegetable intake in late midlife and cognition in later life also comes from the health professionals follow-up study, which showed that higher consumption of both fruit and vegetables was associated with lower odds of poor subjective cognitive function at 18–22-year follow-up[37]. Whilst no objective measure was included in this study, the experience of cognitive function subjectively may be particularly important in terms of quality of life. Performance on cognitive tests assessing memory and executive function improved with an increasing intake of fruit and vegetables in the Hordaland health study, with a marked dose-dependent relationship up to about 500 g/d. When analysed separately, fruit consumption was positively associated with performance on three out of five cognitive tests, whereas vegetable consumption was positively associated with performance on four tests[38]. Interestingly, data from the Boston Puerto Rican health study indicated that greater variety of fruit and vegetable intake but not quantity was associated with better cognition, and this association was strongest for vegetables[39].

Studies that have examined the role of vegetables separately from fruit have shown higher intake to be associated with smaller declines in processing speed and global cognitive function. This is despite vegetable intake being associated with lower information processing speed and worse cognitive flexibility at baseline, which may be driven by negative effects of allium (garlic, onion and leek) consumption[40]. Total vegetable intake was also inversely associated with cognitive decline in the nurses' health study, despite no such association for fruit and vegetables combined. The highest intake of vegetable was equivalent to 1·5 years less decline at the 2-year follow-up[41]. Similarly, those in the highest two quintiles of vegetable intake in the Chicago Health and Aging Project showed a 40 % reduction in decline on a global cognition measure at 6-year follow-up when compared to the lowest quartile intake[42]. Moreover, a specific association between cognitive decline and green leafy vegetables was observed[42,43]. This is supported by the nurses' health study showing the greatest benefit for green leafy vegetables, but also a specific benefit for cruciferous vegetable, particularly for episodic memory[41]. In the Doetinchem cohort study, higher intake of cabbage was associated with better memory and better global cognitive function at baseline, and with smaller decline in information processing speed at 5-year follow-up, whilst root vegetables were associated with smaller declines in cognitive flexibility and global cognition[40]. Support for the roles of root and cruciferous vegetables also comes from the Hordaland health study showing strongest associations for carrots, and cruciferous vegetables, but also for citrus fruits[38].

Effects of specific fruits have been explored with the nurses' health study showing that greater intake of blueberries and strawberries was associated with better episodic memory scores and slower rates of cognitive decline for global cognition, equivalent to up to 2·5 years of ageing[44]. Consumers of avocado were also shown to have better episodic memory and global cognition than non-consumers[45]. Whilst not always categorised as fruit, a specific benefit has also been shown for tree nuts. The Doetinchem cohort study observed that higher nut intake was related to better global cognition, flexibility, memory and processing speed[40]. Long-term (6-year) nut intake was linked to better global cognition in women aged ≥70 years but not with cognitive decline[46] and an association to 5-year cognitive decline in the Doetinchem cohort study was lost following adjustment for cardiovascular risk factors[40]. This indicates a role for cardiovascular effects, which is supported by cognitive improvements shown following Mediterranean diet plus mixed tree nuts in those at high cardiovascular risk[31].

Epidemiological data suggest a relationship between fruit and vegetable intake and cognition. The evidence appears to be stronger for an association between vegetables and cognition than for fruit, which may relate to the common inclusion of fruit juice in the fruit category, despite differences in their fibre content. Since fruit and fruit juice modulate different aspects of immune function, with juice potentially linked to proinflammatory pathway activation[47], the inclusion of fruit juice in the fruit category may be concealing effects of whole fruit. Specific benefits shown for berries, citrus fruits, avocado and nuts suggest fruit is worthy of further investigation in relation to cognition; nuts in particular represent a nutrient-dense food with less sugar than other fruits. In terms of vegetables, a specific benefit may be seen for cruciferous or green leafy vegetables. However, this is not consistently shown with one study showing benefits for both[41], whilst others show benefits for one or the other; a specific benefit for cabbage[40] may indicate that green and leafy vegetables such as kale and savoy cabbage may confer the most favourable effects, potentially due to the high levels of glucosinolates, carotenoids, vitamins, minerals and flavonoids. In an analysis focused on flavonoids, the Lothian birth cohort 1936 study failed to show effects of fruit and/or vegetables[48]. This potentially highlights the importance of covariates in epidemiological research since relationships between vegetable intake and cognition were lost after controlling for childhood IQ, whilst those for total fruit intake were lost with the additional inclusion of smoking, socioeconomic status, education and the apoE 14 allele.

Randomised controlled trials

RCT in this area (see Table 2) have tended to focus on fruit, specifically flavonoid-rich. The effects of orange juice consumption were assessed in a crossover trial of 60–81-year-olds. Cognition was assessed via five episodic memory tasks and six executive function tasks, pre- and post- a 500 ml serving of 305 mg flavanones or placebo for 8 weeks. The findings revealed improvement in global cognitive function, with no effects on episodic memory or executive function when assessed separately[49]. Several studies have also assessed the effects of flavonoid-rich berries. Effects of 12 weeks' tart cherry juice were assessed in 65–80-year-olds on measures of episodic memory, sustained attention, information processing, executive function and subjective memory[50]. Compared to placebo, 480 ml tart cherry juice daily led to fewer errors on an episodic memory task, and shorter movement reaction time, as well as increasing contentment with memory. Two studies have assessed effects of blueberry in older adults[51,52]. Twenty-four g/d freeze-dried blueberry extract (equivalent to one cup of fresh blueberries) led to improved episodic memory and executive function in 60–75-year-olds, with no effects on information processing or attention tasks[51]. Different doses and forms of blueberry have also been assessed in 65–80-year-olds[52]. Effects of 500 and 1000 mg wild blueberry powder and 100 mg of a purified extract were assessed on measures of episodic memory, executive function and selective attention. The purified extract led to improved episodic memory and visual memory span at 12 but not 24 weeks, compared to placebo[52]. Interestingly, the purified extract contained negligible fat, fibre, vitamin C and sugars, which were present in the other blueberry interventions. This indicates that the observed effects are attributable to the flavonoid content alone rather than a synergy with these other components. The lack of effects at 24 weeks is difficult to explain, particularly as systolic blood pressure was reduced at 12 and 24 weeks, but a tentative explanation is that this is reflective of a practice effect whereby improved strategy in performing the tasks has reduced task sensitivity. Twelve weeks' consumption of 4·9 g/d freeze-dried cranberry extract (equivalent to one cup of fresh cranberries) was also shown to improve episodic memory in 50–80-year-olds[53]. Reduced LDL-cholesterol was also shown with some evidence for sex differences in response, as well as increased perfusion in specific regions of the right brain. This is contrary to an earlier study showing no effects of cranberry juice on a range of cognitive measures in healthy older adults[54]. These null findings may be due to the form or dose of cranberry administered, with a 909 ml beverage containing 27 % cranberry juice being delivered, or they could indicate that a 6-week intervention was not sufficient to elicit an effect on cognitive performance in this population.

The effects of cocoa should also be considered here. Whilst not typically thought of as a fruit, cocoa represents the seed of the fruit of the cacao tree and has been studied for potential benefits due to its flavan-3-ol content. In one such study, high flavan-3-ol (993 mg), intermediate flavan-3-ol (520 mg) or low flavan-3-ol control (48 mg) were given for 8 weeks. Improvements to information processing and a measure of executive function were shown following both flavan-3-ol doses and the highest dose also improved verbal fluency[55]. Importantly, no effects were observed on the mini-mental state examination, highlighting the lack of sensitivity of this measure in short

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Table 2. Randomised controlled trials of fruit and vegetable juices and extracts

Reference	Sample	Study design	Intervention	Method of cognitive assessment	Other relevant assessments	Key findings
Babateen *et al.*[36]	*n* 50 (61 % female), overweight or obese older adults (mean age 66 years)	Single- blind, parallel groups, feasibility trial. Tested at baseline and 13 weeks	High dose (800 mg/d), moderate (400 mg/d), low (200 mg/d) or nitrate-depleted beetroot juice	Word presentation, immediate word recall, numeric working memory, choice reaction time, Stroop, digit vigilance, computerised Corsi blocks, peg and ball, delayed word recall, word recognition, trail making test A and B. Combined to create accuracy and speed of: attention, working memory, episodic memory, and global cognition	Cerebral blood flow via quantitative near-IR spectroscopy	No significant effects on cognition or cerebral blood flow
Brickman *et al.*[56]	*n* 37 (73 % female), healthy but sedentary, 50–69 years old (mean age 58 years)	Double-blind, parallel groups. Tested at baseline and 12 weeks	High flavanol – 900 mg of cocoa flavanols (138 mg of epicatechin); or low flavanol control – 10 mg cocoa flavanols (<2 mg epicatechin)	Modified-Benton task	High-resolution functional MRI to map precise site of age-related dentate gyrus function	High flavanol reduced reaction time compared to control and increased cerebral blood volume in dentate gyrus
Chai *et al.*[50]	*n* 37 (54 % female), 65–80 years old (mean age 70 years)	Parallel groups. Tested at baseline and 12 weeks.	Montmorency tart cherry juice (480 ml tart cherry juice, 68 ml Montmorency tart cherry juice concentrate, 412 ml water), consumed twice daily. Placebo matched for carbohydrate content, colour and tartness	Paired associates learning, rapid visual information processing, reaction time test, spatial working memory test, digit span, subjective memory		Compared to placebo, cherry juice increased contentment with memory, reduced movement time, reduced errors in episodic visual memory, improved visual sustained attention and improved working memory
Crews *et al.*[54]	*n* 47 (55 % female), ≥60 years with no history of dementia or neurocognitive impairment (mean age 69 years)	Double-blind, parallel groups. Tested at baseline and 6 weeks	Cranberry juice, sweetened with sucralose. 16 oz consumed twice daily. Placebo matched for appearance, smell, taste, and vitamin C content	Selective reminding test, Wechsler memory scale-III faces I and faces II subtests, trail making test A and B, Stroop colour and word test, Wechsler adults intelligence scale III and digit symbol-coding subtest	Follow-up self-report questionnaire to measures changes over the 6 weeks in: overall ability to remember, thinking abilities, moods, energy levels and overall health	No effects of cranberry juice
Flanagan *et al.*[53]	*n* 60 (58 % female) healthy older adults (mean age 65·5 years)	Double-blind, parallel groups. Tested at baseline and 12 weeks	Freeze-dried cranberry extract, 4·5 g sachet consumed twice daily, equivalent to 100 g fresh cranberries. Placebo matched for taste, colour, fructose, total sugar and energy	Addenbrooke's cognitive examination III – composite global cognition, executive function and verbal episodic memory. Trail making test, digit span, Rey complex figure test. Supermarket test	MRI brain scans and blood measures of polyphenol metabolites	Cranberry extract improved episodic memory, compared to placebo and increased perfusion in key cerebral regions supporting memory consolidation and retrieval

Table 2. (*Cont.*)

Reference	Sample	Study design	Intervention	Method of cognitive assessment	Other relevant assessments	Key findings
Kean *et al.*[49]	*n* 37 (65 % female) healthy older adults (mean age 67)	Double- blind, crossover. Each treatment consumed for 8 weeks with a 4-week washout	Orange juice drink either containing high flavanones (305 mg/d) or low flavanones (37 mg/d)	Go-NoGo, CERAD (Consortium to Establish a Registry for Alzheimer's Disease) immediate and delayed recall, letter memory, verbal paired associates, serial sevens, spatial working memory, digit symbol substitution test, letter fluency. Tasks grouped into two domains: episodic memory and executive function		Global cognitive function better after flavanone-rich juice, compared to low flavanone juice. High flavanone juice attenuated general decline in cognitive performance
Mastroiacovo *et al.*[55]	*n* 90 (59 % female) elderly (mean age 65 years)	Double-blind, parallel groups. Tested at baseline and 8 weeks	Dairy-based cocoa drink; high flavanol (993 mg serving), intermediate flavanol (520 mg serving) and low/control flavanol (48 mg serving)	Mini-mental state exam, trail making tests A and B, verbal fluency test. Overall cognitive function also calculated	Blood pressure at each testing visit and blood sample to measure lipid profile, fasting plasma glucose and insulin	Cocoa flavanols consumed for 8 weeks improved cognitive function, blood pressure and metabolic markers. Change in insulin resistance predicted cognitive change
Miller *et al.*[51]	*n* 37 (68 % female) adults aged 60–75 years (mean age 67 years)	Double-blind, parallel groups. Tested at baseline, 6 weeks and 12 weeks	Blueberry freeze-dried extract. 12 g consumed twice daily, equivalent to one cup of fresh blueberries. Placebo consisting of colour matched blueberry flavoured placebo powder	Task switching test, trail making test, California verbal learning test, digit span test, virtual Morris water maze attention and attention network task	Geriatric depression scale and profile of mood states. Mobility assessment via dynamic stance and gait analysis	Blueberry led to reduced repetition errors on word list recall and increased accuracy during task switching at 12 weeks
Neshatdoust *et al.*[57]	*n* 40 (45 % female) healthy older adults (mean age 68 years)	Double- blind, crossover. Each treatment consumed for 4 weeks with a 4-week washout	High-flavanol cocoa drink (494 mg total flavanols) or low-flavanol drink (23 mg total flavanols). Standardised for their macro- and micro-nutrient content, energy, theobromine and caffeine content	Go-NoGo task, Stroop, plus-minus, trail making tasks, letter memory task, free and delayed recall, word and face recognition, serial sevens, spatial delayed recall task, virtual 3D radial arm maze task, word stem completion task, digit symbol substitution task and rapid visual information processing	Serum brain-derived neurotrophic factor (BDNF)	High flavanol led to increased global cognitive function and increased serum BDNF levels
Whyte *et al.*[52]	*n* 122 (61 % female), healthy adults aged 65–80 (mean age 70 years)	Double-blind, parallel groups. Tested at baseline, 12 and 24 weeks	Wild blueberry powder 500 mg, wild blueberry powder 1000 mg, wild blueberry extract 100 mg and placebo powder (consisting of maltodextrin and food-grade artificial dye) colour-matched to treatment	Rey auditory verbal learning task, object recognition task, Corsi blocks, Sternberg memory scanning task, modified attention network task and Stroop task	Positive and negative affect schedule-NOW to determine mood. Blood pressure and heart rate taken after the first half of the cognitive task battery	Purified blueberry extract improved episodic memory and visual memory span at 12 but not 24 weeks. Systolic blood pressure reduced at 12 and 24 weeks

intervention trials of healthy adults. This study also attempted to ascertain the determinants of cognitive change, observing that insulin resistance explained 17 % of cognitive change. Systolic blood pressure and lipid peroxidation were not predictors despite blood pressure and several metabolic markers being improved by the intervention. Another interesting study of cocoa showed that high flavan-3-ol (900 mg) improved novel object recognition reaction time when compared to control. Moreover, the authors reported that the improvement observed following intake of high flavan-3-ol cocoa for 12 weeks was equivalent to three decades of ageing, shifting the slope in expected age-related decline. Imaging data also showed an increase in cerebral blood volume in the dentate gyrus region of the hippocampus and this increase was inversely correlated with reaction time. This indicates a potential mechanism of action for improvements linked to increased blood flow, which may be specific to the hippocampus given the localised effect and the role of the hippocampus in the task assessed[56]. Significant improvements to global cognition were also observed in healthy elderly following supplementation with 494 mg of cocoa flavan-3-ol for 28 d. Interestingly, increases in serum brain-derived neurotrophic factor levels were also observed[57].

Studies of nuts have produced mixed findings. In the dual-centre walnuts and healthy ageing study there were no effects of a 2-year walnut intervention[58]. However, a site-specific improvement to global cognition and functional MRI differences indicative of improved neural efficiency in the walnut group were observed following 30–60 g/d walnuts over 2 years. A study assessing effects of 12-week almond consumption failed to find effects on cognition when compared to an isoenergetic carbohydrate-rich snack in overweight and obese older adults, despite improvements to aspects of cardiometabolic health[59]. However, 12-week peanut consumption was observed to enhance memory, verbal fluency and processing speed, as well as increasing cerebrovascular reactivity and small artery elasticity in healthy overweight adults[60]. Changes in cerebrovascular reactivity in the left middle cerebral artery were also positively correlated with changes in delayed memory and recognition. Although peanuts are legumes and therefore classified as vegetables, they are usually considered in the nut category due to their composition. These nut studies illustrate the issue of implementing a control in studies of whole foods. In two of the studies the control arm consisted of habitual diet minus nuts[58,60], whereas in the other study nuts were compared to an isoenergetic snack[59]. The first option presents issues in that no intervention is present in the control arm, whereas the snack comparator makes interpreting findings difficult due to potential effects of the composition of the control employed.

RCT of vegetables are less prevalent than fruit, possibly due to the logistics of developing a control for the intervention. Fruit is typically studied in juice form, but vegetable juice is less commonly consumed and is potentially less likely to be accepted by participants where daily intake is required. For instance, there are a number of studies of beetroot juice, but only one of these has included repeated consumption in healthy older adults[36]. A 13-week trial in overweight and obese older adults assessed effects of high (800 mg/d), moderate (400 mg/d) and low (200 mg/d) nitrate administered in beetroot juice and compared effects to a nitrate-depleted beetroot juice. Despite a wide array of cognitive tasks, there was no evidence of any effects of beetroot juice on cognition, and no effects on cerebral blood volume as assessed with near IR spectroscopy. This study was designed as a feasibility study and not intended to provide a definitive investigation of the effects of nitrate on cognition and cerebral blood flow, but the null findings are unexpected based upon the available evidence from short-term studies.

Evidence for cognitive benefits of fruit and vegetables from RCT is weaker than epidemiological data. There are generally only one or two RCT per food type, with the strongest evidence for cocoa where three studies exist. Although the available data are limited, the findings are generally positive despite potential issues with short duration of intervention and limited knowledge of optimal dosage. Not all studies show positive effects, the dual-centre walnuts and healthy ageing study[58] failed to detect effects of a 2-year walnut intervention when analysed in the population as whole. However, subgroup analysis revealed a site-specific improvement. Compared with other sites, participants at the site where improvement was observed, reported lower education and lower intake of the plant *n*-3, α-linolenic acid[58]. These findings potentially suggest that those at risk, either due to poorer nutrition or poorer education, may be more susceptible to cognitive improvements following a fruit or vegetable intervention. A number of studies[53,55,56,60] indicate increased cerebral blood volume following fruit/legume intervention, as well as improved cardiometabolic markers, and in some cases a correlation between changes in cognition and cerebrovascular/metabolic markers. These findings may suggest that cognitive improvement is more likely in those who are at risk for cardiometabolic dysfunction.

However, RCT assessing effects of diet on cognition often impose strict exclusion criteria such as: no clinically significant coexisting medical conditions, including CVD, cerebrovascular events, neurological disorders, inflammatory diseases, metabolic disorders, gastrointestinal abnormalities, mental illness including depression; no prescription medication; no supplements; no current smokers; no individuals with BMI $\geq$30 kg/m^2. Whilst these criteria are sensible in terms of study design and minimising ‘noise’ from uncontrolled variables, they present a problem in terms of representativeness. For instance, 63 % of adults in England aged 65–74 reported a longstanding health condition in 2018[61]. In adults aged $\geq$65, at least 80 % were shown to have taken a prescribed medication in the past week, and more than one in ten took at least eight different prescribed medications per week[62]. Whilst 75 % of 65–74-year-olds were reported to be overweight or obese[61]. In addition to problems relating to generalisability of findings, these studies create somewhat of a paradox in that they are exploring

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the importance of nutrition to health yet recruiting unusually healthy people whilst assuming suboptimal nutrition that can be enhanced by intervention.

Nutrition status and self-selection

Inclusion of nutrition status measures, such as dietary intake measures and nutritional biomarkers, in RCT of nutrition interventions on cognition is increasing, but still rare. Failure to measure nutritional status in cognitive studies presents obvious problems in not being able to ascertain if any null findings are due to already optimal status in study participants[63]. Indeed, post-hoc analyses indicate that beneficial effects of vitamins A, C and certain B-vitamins on cognitive decline may only be shown in those with low baseline intake (for a review see[64]). However, due to self-selection bias, those who volunteer for RCT of nutrition are likely to be health conscious and potentially less likely to display suboptimal nutrition. This is nicely illustrated by the memory and attention supplementation trial where a validated (against blood markers) questionnaire was used to assess diet quality prior to enrolment, aiming for 50 % 'optimal' diet (a high intake of fruit, vegetables, legumes, olive oil and nuts, and a lower intake of processed foods) and 50 % suboptimal. Out of 501 volunteers, 461 (74·4 %) met the criterion for an 'optimal' diet indicative of elevated nutrient status[65]. When considered against the statistic that only 5·4 % of Australian adults meet the current recommendations for both fruit and vegetable intake, this again highlights the lack of representativeness of cognition-nutrition research volunteers. Since multivitamin use is more common in females and those with healthier lifestyle habits, higher educational attainment, higher socioeconomic status and of lower BMI[66], it is potentially more likely that those who participate in nutrition research will share similar characteristics. This is supported by evidence from the Monongahela Valley Independent Elders Survey, where those who volunteered to participate were more likely to be women, and had more formal years of education, higher cognitive test scores, higher instrumental activities of daily living ability and lower mortality rates than randomly selected participants[67]. This indicates a further issue with cognitive reserve since those with more years of formal education and who engage in more physical activity are at reduced risk of cognitive decline[68]. Higher cognitive test scores in those who volunteer may also indicate the presence of ceiling effects in study participants, again increasing the likelihood of null findings.

Conclusions

There is growing evidence for an association between fruit and vegetable intake and cognitive function, but this is not always consistent. Some of the differences observed in findings may relate to the populations studied, but also the measures used to assess fruit and vegetable intake – for instance a fruit and vegetable-specific FFQ *v.* simply asking how many portions of fruit and vegetable are consumed daily, as well as the covariates included in the analyses. Nevertheless, epidemiological support for beneficial effects of fruit and vegetables tends to be stronger than that from RCT. This is not uncommon and is to be expected given the limited information available on dose and duration required to see a measurable effect in RCT. This is further complicated in older populations who may experience issues with absorption of certain micronutrients[69]. Restrictive inclusion/exclusion criteria may also impact findings since those who meet these requirements are likely to be already consuming a healthy diet and may not benefit from additional nutrient intervention. Given the large proportion of older adults who consume a suboptimal diet and who suffer ill health, it is imperative that steps are taken to ensure inclusion in RCT of those most at risk for cognitive decline, who are most likely to receive the greatest benefit. Racial diversity is also lacking in studies of nutrition and cognition, and this is particularly important when considering that race has been shown to modify relationships between cardiovascular factors and cognition[11] and between nutrition and cognition[70]. Sex has also been observed to modify the relationship between nutrition and cognition[70], and sex differences in cognition[71,72], nutrient requirements[73] and in pathways by which dietary nutrients and gut microbes modify metabolism and immunity[74] all indicate that sex effects should be considered in dietary interventions on cognition, but rarely are. This is particularly important in older adults due to the impact of menopause but also the higher prevalence of dementia in women than men[75]. Data showing that an increment of 100 g daily of fruit and vegetable consumption is related to approximately 13 % reduction in dementia risk[76] highlights the importance of research in this field and the necessity to ensure that those most at risk are included in this research. This review highlights epidemiological evidence for a relationship between fruit and vegetable intake and cognition, which appears to be stronger for vegetables than fruit. However, RCT exploring effects of vegetables on cognition are lacking. Further research is required exploring effects of a range of different fruits and vegetables, including different forms of fruits and vegetables, on cognition, particularly in those at risk for cognitive decline.

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Conflict of Interest

None.

Authorship

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